UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/729,895 | 12/05/2003 | Cheryl L. Willman | N12-038US | 2100 |

28156 7590 02/08/2007

COLEMAN SUDOL SAPONE, P.C.
714 COLORADO AVENUE
BRIDGE PORT, CT 06605-1601

| EXAMINER | |
|---|---|
| GODDARD, LAURA B | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/08/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/729,895 | WILLMAN ET AL. | |
| | Examiner | Art Unit | |
| | Laura B. Goddard, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above claim(s) *4-6,9-13 and 16-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7,8,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The Election filed November 13, 2006 in response to the Office Action of Sept 7, 2006 is acknowledged. Applicant elected with traverse Group I, claims 1-3, 7, 8, 14, and 15, drawn to an OPAL1 splice variant polynucleotide SEQ ID NO:1 and a nucleic acid encoding the polypeptide SEQ ID NO:2.

2. Applicants traverse the restriction between the OPAL1 splice variant nucleic acid SEQ ID NO:1 and the corresponding encoded protein SEQ ID NO:2. Applicants traverse the restriction requirement between the polynucleotides SEQ ID NO:1 and 3, as well as the corresponding polypeptides SEQ ID NO:2 and 4. Applicants argue that the polynucleotides and the polypeptides corresponding thereto are so closely related that they may be examined together with a significant degree of administrative efficiency and because identical claims are readable on the two "species". Applicants argue that the presentation of the originally filed claims would not place a serious burden on the Examiner as to require restriction, and that all of the originally filed claims are related, thought patentably distinct products or process have common utility. All the inventions are searchable in both the same class 536 and 530 and subclasses 23.1 and 350 (p. 1-3).

The arguments have been considered but are not found persuasive because the splice variants SEQ ID NO:1 and 3 are structurally and functionally distinct polynucleotides representing different splice variants of OPAL1. They are not species,

as Applicants refer to them as, but rather, are independent and distinct inventions representing independent and distinct polynucleotides that encode structurally distinct proteins. A search of each of these splice variants would not be coextensive and would invoke a high burden of search because they are structurally and functionally different. Further, the polynucleotides and corresponding polypeptides are in different classes, requiring different searches. As stated in the previous Office Action (p. 15-16): "The DNA of Group 1 is related to the protein of Group 2 by virtue of the fact that the DNA codes for the protein. The DNA molecule has utility for the recombinant production of the protein in a host cell. Although the DNA and the protein are related, since the DNA encodes the specifically claimed protein, they are distinct inventions because the protein product can be made by other and materially distinct processes, such as purification from the natural source. Further, DNA can be used for processes other than the production of protein, such as nucleic acid hybridization assays.

Furthermore, searching the inventions of Groups 1 and 2 together would impose a serious search burden. In the instant case, the search of the polypeptides and polynucleotides are not coextensive. The inventions of Groups 1 and 2 have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate database. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequences of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had

no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. The scope of polynucleotides as claimed extend beyond the polynucleotide that encodes the claimed polypeptides as explained above, furthermore, a search of the nucleic acid molecules of Group 1 would require an oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptide of Group 2. As such, it would be burdensome to search the inventions of Groups 1 and 2."

For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

3. Claims 1-78 are pending. Claims 4-6, 9-13, and 16-78 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1-3, 7, 8, 14, and 15, as drawn to SEQ ID NO:1 and a polynucleotide encoding SEQ ID NO:2, are currently under prosecution.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The use of laboratory designations only to identify a particular

protein or polynucleotide such as "**G1**" or "**G2**" renders the claims indefinite because different laboratories may use the same laboratory designation to define completely distinct proteins or polynucleotides. For example, Hussein et al (J of Clinical Microbiology, 1993, 31:2491-2496) use the terms "G1" and "G2" to define serotypes of rotavirus (see abstract and p. 2491, col. 1). Mariott et al (Virology, 1992, 190:606-615; abstract only) and Padula et al (J of General Virology, 2002, 83:2117-2122) use the terms "G1" and "G2" to refer to bunyavirus glycoproteins. Amendment of the claims, for example, to include the **SEQ ID number** which unambiguously defines a given protein or polynucleotide, would obviate the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 7, 8, 14, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to an isolated OPAL1 polynucleotide comprising a nucleotide sequence from the group consisting of: (b) **a complement** of SEQ ID NO:1, (d) **a nucleotide sequence that hybridizes** to SEQ ID NO:1, (e) **a nucleotide having**

**at least 95% identity** to SEQ ID NO:1, (f) **a nucleotide having at least 98% identity** to SEQ ID NO:1, and (g) **a nucleotide sequence encoding a polypeptide** encoded by SEQ ID NO:2 (claim 1), an expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence (claim 7), a host cell transformed or transfected with an expression vector according to claim 7 (claim 8), a pharmaceutical composition comprising a therapeutic agent, polynucleotide of claim 1 (claim 14), the pharmaceutical composition of claim 14 further comprising a second therapeutic agent (claim 15).

With regards to a polynucleotide that hybridizes to SEQ ID NO:1, the claims are drawn to any and all naturally occurring DNA molecules that hybridize to SEQ ID NO:1 under a wide range of conditions. This would include a substantial number of nucleic acids that have a low percent sequence identity to SEQ ID NO:1 when hybridized under low to moderate stringency conditions and would include nucleic acids that encode for proteins or fragments thereof that do not possess the biological activity of SEQ ID NO:1. With regards to a polynucleotide that is a complement of SEQ ID NO:1, the claims are broadly drawn to any size polynucleotide that forms a complement to any portion of SEQ ID NO:1 and includes polynucleotides that have a low percent sequence identity to SEQ ID NO:1 and would include nucleic acids that encode for proteins or fragments thereof that do not possess the biological activity of SEQ ID NO:1. With regards to "**a** nucleotide sequence having at least 95% or 98% identity to SEQ ID NO:1", the claims are broadly drawn to a polynucleotide or fragment of unknown length and sequence that shares at least 95% or 98% identity to SEQ ID NO:1. With regards to "**a** nucleotide

sequence encoding a polypeptide encoded by SEQ ID NO:2", the claims are broadly drawn to a polynucleotide or fragment of any length that encodes any polypeptide of any length of SEQ ID NO:2, and is not limited to polynucleotides that encode full-length SEQ ID NO:2.

The specification discloses SEQ ID NO:1 as a splice variant polynucleotide named OPAL1, which encodes polypeptide SEQ ID NO:2 (p. 8, lines 17-21; Figure 2; p. 23, lines 3-6). Full-length OPAL1 is represented by SEQ ID NO:16 (p. 8, lines 24-25; Fig. 2C). The specification discloses that the novel gene OPAL1 has been found to be strongly predictive of outcome in childhood leukemia and presents new opportunities for better diagnosis, risk classification, and better therapeutic options (p. 6, lines 29-31; p. 14, lines 12-31). The specification discloses that a "complement" refers to the ability of two single stranded polynucleotides to base pair with each other (p. 25, lines 27-34). The specification discloses that "hybridizes" means that a single stranded polynucleotide forms a non-covalent interaction with a complementary polynucleotide under certain conditions (p. 26, lines 2-10). The specification does not disclose complements of SEQ ID NO:1, nucleotide sequences that hybridize to SEQ ID NO:1, nucleotides having at least 95% identity to SEQ ID NO:1, nucleotides having at least 98% identity to SEQ ID NO:1, or nucleotide sequences encoding polypeptides encoded by SEQ ID NO:2 as broadly encompassed in the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial

structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "(b) a complement of SEQ ID NO:1, (d) a nucleotide sequence that hybridizes to SEQ ID NO:1, (e) a nucleotide having at least 95% identity to SEQ ID NO:1, (f) a nucleotide having at least 98% identity to SEQ ID NO:1, and (g) a nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:2". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can

> do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description of complements of SEQ ID NO:1, nucleotide sequences that hybridize to SEQ ID NO:1, nucleotides having at least 95% identity to SEQ ID NO:1, nucleotides having at least 98% identity to SEQ ID NO:1, or nucleotide sequences encoding polypeptides encoded by SEQ ID NO:2, per Lilly by structurally describing representative polynucleotides or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe complements of SEQ ID NO:1, nucleotide sequences that hybridize to SEQ ID NO:1, nucleotides having at least 95% identity to SEQ ID NO:1, nucleotides having at least 98% identity to SEQ ID NO:1, or nucleotide sequences encoding polypeptides encoded by SEQ ID NO:2 useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses OPAL1 splice variant polynucleotide SEQ ID NO:1, this does not provide a description of the broadly claimed complements of SEQ ID NO:1, nucleotide sequences that hybridize to SEQ ID NO:1, nucleotides having at least 95% identity to SEQ ID NO:1, nucleotides having at least 98% identity to SEQ ID NO:1,

or nucleotide sequences encoding polypeptides encoded by SEQ ID NO:2 that would satisfy the standard set out in Enzo because the specification provides no functional characteristics coupled to structural features.

Further, the specification also fails to describe complements of SEQ ID NO:1, nucleotide sequences that hybridize to SEQ ID NO:1, nucleotides having at least 95% identity to SEQ ID NO:1, nucleotides having at least 98% identity to SEQ ID NO:1, or nucleotide sequences encoding polypeptides encoded by SEQ ID NO:2, by the test set out in Lilly because the specification describes only SEQ ID NO:1. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of complements of SEQ ID NO:1, nucleotide sequences that hybridize to SEQ ID NO:1, nucleotides having at least 95% identity to SEQ ID NO:1, nucleotides having at least 98% identity to SEQ ID NO:1, or nucleotide sequences encoding polypeptides encoded by SEQ ID NO:2 that is required to practice the claimed invention.

6. Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of compounds referred to "a compound that alters the activity of a G1 or G2 polypeptide". Therefore, the claims encompass a genus of molecules defined solely by

its principal biological property, which is simply a wish to know the identity of any material. This is a WRITTEN DESCRIPTION rejection.

The claim is drawn to the pharmaceutical composition of claim 14 further comprising a second therapeutic agent (iii) **a compound that alters the activity of a G1 or G2 polypeptide**.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification discloses that G1 is also referred to as "G protein β2, related sequence 1" and that G2 is referred to as "IL-10 Receptor alpha" (p. 11, lines 28-31).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of

"a compound that alters the activity of a G1 or G2 polypeptide". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics .... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of

such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb.13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of compounds that alter the activity of a G1 or G2 polypeptide nor does it provide a description of structural features that are common to the genus of compounds. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus as broadly claimed. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled m the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the

skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of compounds that alter the activity of a G1 or G2 polypeptide, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the specification fails to adequately describe "compounds that alter the activity of a G1 or G2 polypeptide". Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 9112 is severable from its enablement provision (see page 1115).

7. Claims 8, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a **host cell** transformed or transfected with an expression vector according to claim 7 (claim 8), a **pharmaceutical** composition comprising a therapeutic agent, polynucleotide of claim 1 (claim 14), and the **pharmaceutical** composition of claim 14 further comprising a second therapeutic agent selected from the group consisting of: (i) a polynucleotide encoding G1 or G2, (ii) a G1 or G2 polypeptide, or (iii) a compound that alters the activity of a G1 or G2 polypeptide (claim 15).

Claim 8 encompasses a transformed "host cell" *in vivo* which reasonably read on the transfection of intact hosts and mammalian hosts with the claimed vector. The term "pharmaceutical" reasonably reads on a composition with treatment capabilities.

The specification discloses that gene therapies can be used to increase the amount of a polypeptide of interest such as OPAL1/G0 in a host cell of a patient. Polynucleotides operably encoding the polypeptide of interest can be delivered to a patient either as "naked DNA" or as part of an expression vector (p. 19, lines 19-22). The specification discloses pharmaceutical compositions and administration for treatment of leukemia on page 21, line 16-p. 22, line 2.

One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification does not provide guidance or examples for the claimed polynucleotides or compositions functioning as a pharmaceutical. Holleman et al (Blood, 2006, 108:1984-1990) teach that the function of OPAL1/G0 is unknown, and a search of the prior and current art does not enable OPAL1/G0 polynucleotides or further comprising G1, G2 polynucleotides, polypeptides, or compounds altering any activities of GI or G2 to function as a pharmaceutical for any disorder.

*In re Brana 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995)* demonstrates the criteria needed for enablement of a claimed product for pharmaceutical use. The Applicants in *In re Brana* claimed a chemical compound capable of treating cancer, wherein the chemical compound was structurally similar to known compounds that have known *in vivo* use to treat tumors, and more importantly, the Applicant provided *in vivo* data that the claimed compound could treat tumors in mice, hence the claimed chemical

compound was enabled for treating tumors. In the instant application, unlike in *In re Brana*, the claimed OPAL1 polynucleotide has unknown function, and a search of the current art does not teach or enable an OPAL1 polynucleotide or composition comprising OPAL1 polynucleotide and G1 or G2, or compounds that alter any activity of G1 or G2, used successfully to treat leukemia or as a pharmaceutical *in vivo.* Additionally, the instant application, unlike in *In re Brana*, does not provide examples or guidance for any pharmaceutical *in vivo* data, particularly regarding the treatment of leukemia. Hence, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Further, Rolland (Advanced Drug Delivery Reviews, 2005, 57:669-673), teach the unpredictability and limitations of gene therapy. Tissue distribution and persistence

of expression plasmids is dependent on several parameters, including the route of administration, the formulation, and the use of a device. For instance, DNA can be detected in all major organs after intramuscular injection, with rapid clearance from all those tissues with the exception of the injection site. Intravenous (systemic) and intratumoral have shown a far more rapid elimination from the injected compartment, ranging from minutes to days. To date, there is a void of plasmid pharmacokinetic data in humans, thus making it impossible to evaluate the predictability of the animal models (p. 671, cols. 1 and 2). Rolland teach that DNA plasmids have many barriers to overcome for efficient gene transfer and expression. Following passive or active distribution of plasmids to target tissues after *in vivo* administration and uptake by the cells, plasmids need to be able to navigate through the cell cytoplasm before reaching the nucleus where gene expression can be initiated. This intracellular trafficking of plasmids remains a poorly understood series of events, making the rational design of delivery elements to overcome those rate-limiting steps a major challenge. At the end of the DNA plasmid's journey from the site of administration to the nucleus of the transfected cell, the plasmid expression system needs to be functional and contain specific elements for gene expression to occur at the appropriate levels, with the tight specificity and accuracy, and for an adequate period of time (p. 672, col. 1). McCormick (Nature Reviews, 2001, 1:130-141) teaches the challenges of gene therapy including the need for a vector or virus delivering the nucleic acid to avoid neutralization by the immune system, the rapid clearance of systemically administered agents from the bloodstream by the liver, and if the agent survives that, the agent must leak from the

blood vessels into tumors and spread within the heterogeneous mass of the tumor (p. 137, col. 2). McCormick teaches that although the biological principles of cancer gene therapy are sound, translating these principles into reality remains a formidable-perhaps prohibitive- challenge (p. 138, col. 2). Clearly, the art teaches the complexity and unpredictability of DNA therapy.

MPEP 2164.03 states: The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. Given the state of the art, one of skill in the art could not predictably use the claimed polynucleotide or composition to function predictably as a pharmaceutical or for gene therapy.

Therefore, in view of the state of the art, the unpredictability in the art, the breadth of the claims, lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1, 7, 8, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/66689 A2, Tang et al, published 9/13/2001, filed 3/5/2001 (see sequence search Result #6, Geneseq database for a polynucleotide encoding SEQ ID NO:2; and Result #5, Geneseq Database for polynucleotide SEQ ID NO:1).

The claims are drawn to an isolated OPAL1 polynucleotide comprising a nucleotide sequence from the group consisting of: (b) a complement of SEQ ID NO:1, (c) a subunit of SEQ ID NO:1 consisting of at least 60 contiguous nucleotides, (d) a nucleotide sequence that hybridizes to SEQ ID NO:1, (e) a nucleotide having at least 95% identity to SEQ ID NO:1, and (g) a nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:2 (claim 1), an expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence (claim 7), a host cell transformed or transfected with an expression vector according to claim 7 (claim 8), and a pharmaceutical composition comprising a therapeutic agent, polynucleotide of claim 1 (claim 14).

Tang et al teaches a polynucleotide, SEQ ID NO:32, that has 97.6% identity with SEQ ID NO:1 of the instant application (see Result #5, Geneseq Database for polynucleotide SEQ ID NO:1). Tang et al teach polynucleotides that hybridize to SEQ ID NO:32 (p. 3, lines 14-23; p. 15, lines 33-35 to p. 16, lines 1-7), complements of SEQ ID NO:32 (p. 18, lines 7-11). Because SEQ ID NO:1 and SEQ ID NO:32 share 97.6% identity, it is expected that nucleic acids that hybridize to SEQ ID NO:32 would also hybridize to SEQ ID NO:1 and complements of SEQ ID NO:32 include complements to SEQ ID NO:1. The polynucleotide taught by Tang et al comprises a subunit of SEQ ID NO:1 consisting of at least 60 contiguous nucleotides. The polynucleotide taught by Tang et al encodes a polypeptide with 99.7% identity to SEQ ID NO:2 of the instant application (see sequence search Result #6, Geneseq database for a polynucleotide encoding SEQ ID NO:2), hence the polynucleotide taught by Tang et al would encode **a** polypeptide encoded by SEQ ID NO:1. Tang et al an expression vector comprising the polynucleotide operably linked to an expression control sequence (p. 11, line 30 through p. 12, line 15; p. 18, line 29 through p. 19, line 35). Tang et al teach host cells transformed or transfected with the polynucleotide (p. 3, lines 32-4; p. 4, lines 4-5). Tang et al teach a composition comprising the polynucleotide and a pharmaceutically acceptable carrier (p. 4, lines 1-3).

9. Claims 1-3, 7, 8, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 01/94391 A2, Yue et al, published 12/13/2001, filed 6/7/2001 (see sequence search Result # 2, Geneseq database, for SEQ ID NO:1; see Result #1, GenEmbl

database, for SEQ ID NO:1; see Result #2, Geneseq database, for a polynucleotide that encodes SEQ ID NO:2; see Result # 1, GenEmbl database, for a polynucleotide that encodes SEQ ID NO:2).

The claims are drawn to an isolated OPAL1 polynucleotide comprising a nucleotide sequence from the group consisting of (a) SEQ ID NO:1, (b) a complement of SEQ ID NO:1, (c) a subunit of SEQ ID NO:1 consisting of at least 60 contiguous nucleotides, (d) a nucleotide sequence that hybridizes to SEQ ID NO:1, (e) a nucleotide having at least 95% identity to SEQ ID NO:1, (f) a nucleotide having at least 98% identity to SEQ ID NO:1, and (g) a nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:2 (claim 1), an expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence (claim 7), a host cell transformed or transfected with an expression vector according to claim 7 (claim 8), and a pharmaceutical composition comprising a therapeutic agent, polynucleotide of claim 1 (claim 14).

Yue et al teach a polynucleotide, ISIGP-2 (also AAI72318 or SEQ ID NO:7), that shares 100% identity with SEQ ID NO:1 of the instant application. ISIGP-2 also encodes a polypeptide with 100% identity to SEQ ID NO:2 of the instant application. Yue et al teach polynucleotides complementary to ISIGP-2 (p. 8, line 31 through p. 9, line 3), polynucleotides comprising at least 60 contiguous nucleotides of ISIGP-2 (p. 9, lines 1-3), and polynucleotides hybridizing to IGISP-2 (p. 29, lines 26-30; p. 30, lines 7-12). Yue et al teach a composition comprising IGISP-2 and a pharmaceutically acceptable excipient (p. 9, lines 33-34). Yue et al teach a recombinant expression vector

comprising the polynucleotide operably linked to an expression control sequence (p. 31, line 28 through p. 32, line 5; p. 33, line 1 through p. 35, line 22). Yue et al teach host cells transformed or transfected with the polynucleotide (p. 31, lines 28-30; p. 36, lines 11-12; p. 33, line 24 through p. 36, line 15).

10. Claims 1, 7, 8, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,979,557, Isogai et al, issued 12/27/2005, filed 3/12/2002 (see Result #1, issued patents database, sequence search for polynucleotide encoding SEQ ID NO:2; and see Result #1, issued patents database, search for SEQ ID NO:1).

The claims are drawn to an isolated OPAL1 polynucleotide comprising a nucleotide sequence from the group consisting of: (b) a complement of SEQ ID NO:1, (c) a subunit of SEQ ID NO:1 consisting of at least 60 contiguous nucleotides, (d) a nucleotide sequence that hybridizes to SEQ ID NO:1, (e) a nucleotide having at least 95% identity to SEQ ID NO:1, and (g) a nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:2 (claim 1), an expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence (claim 7), a host cell transformed or transfected with an expression vector according to claim 7 (claim 8), and a pharmaceutical composition comprising a therapeutic agent, polynucleotide of claim 1 (claim 14).

Isogai et al teach a polynucleotide, SEQ ID NO:823 (see Table 1, col. 17, lines 31), with 99.7% identity to SEQ ID NO:1 of the instant application, which encodes a polypeptide with 99.6% identity to SEQ ID NO:2 of the instant application. Isogai et al

teach complements of SEQ ID NO:823 (col. 4, lines 36-43; col. 31, line 63 through col. 32, line 8) and polynucleotides hybridizing to SEQ ID NO:823 (col. 4, lines 7-12; col. 30, lines 37-67). Because SEQ ID NO:1 and SEQ ID NO:832 share 99.7% identity, it is expected that nucleic acids that hybridize to SEQ ID NO:823 would also hybridize to SEQ ID NO:1 and complements of SEQ ID NO:823 include complements to SEQ ID NO:1. The polynucleotide taught by Isogai et al comprises a subunit of SEQ ID NO:1 consisting of at least 60 contiguous nucleotides. The polynucleotide taught by Isogai et al encodes a polypeptide with 99.6% identity to SEQ ID NO:2 of the instant application, hence the polynucleotide taught by Isogai et al would encode **a** polypeptide encoded by SEQ ID NO:1. Isogai et al teach a recombinant expression vector comprising the polynucleotide operably linked to an expression control sequence (col. 29, lines 39-57; col. 33, lines 1-45). Isogai et al teach host cells transformed or transfected with the polynucleotide (col. 29, lines 41-58; col. 33, lines 45-57).

11. **Conclusion:** No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600